REMARKS

Claims 1-11 and 15-31 are pending in the instant application.

Obviousness-Type Double Patenting

Claims 1-11, 15, 16, and 22-31 stand rejected under the judicially created doctrine of obviousness-type double patenting over copending applications serial numbers 08/785,977 and 08/788,882 in view of Felgner et al, U.S. Patent 5,580,859. A provisional terminal disclaimer will be filed upon a finding that the present application is otherwise in condition for allowance, should those applications still be pending with claims requiring disclaimer.

Examiner's Objection

Claims 22, 23, 28 and 31 were objected to because "one or more immunogenic polypeptides" was not in the plural form. The instant amendments to claims 22, 23, 28 and 31 have placed the claim in proper form, by the addition of the plural "polypeptides" to the respective claims.

Rejection Under 35 U.S.C. § 112, Second Paragraph

1. Claims 3-11, 15-16, and 23-27 were rejected as indefinite since the phrase "thereby reducing the HDL concentration" in step (b) was contradictory to the preamble statement of the claim, a process for increasing the concentration of HDL. The instant amendment to claim 3 (from which the other rejected claims depend) corrects the clerical error, and requires the limitation of increasing the HDL concentration in step (b).
2. Claims 6, 8-11, 15 and 24 were rejected as indefinite because there was no longer antecedent basis for "said immunogenic peptide" previously recited in

claim 3. Claims 6, 8-11, 15 and 24 have been amended to recite "one or more immunogenic peptides" in conformity with claim 3, thus obviating this rejection.

3. Claim 2 was rejected as indefinite because it was not clear whether the CETP in the blood of claim 2 referred to endogenous CETP or recombinantly expressed CETP. Claim 2 has been amended to be dependent on claim 3 and to set out that the CETP is endogenous. Claim 1 has also been amended to include the limitation of "endogenous CETP" in the blood of the mammal.

4. Claims 1-11 and 15-28 were rejected as indefinite because claims 1 and 3 recite a recombinant DNA molecule which is dissolved or dispersed in a vehicle, but it was unclear how individual nucleotides could be dissolved or dispersed in a vehicle. The amendments to claims 1, 3, and 17 now all require containing a recombinant DNA (as opposed to "dissolved or dispersed"). It is believed that any indefiniteness found in the claims is therefore obviated by this amendment.

Rejection Under 35 U.S.C. § 112, First Paragraph

1. Claims 1, 3, and 17 were rejected under 35 U.S.C. § 112, first paragraph as containing new matter, in that the Examiner states that the specification does not disclose nor contemplate more than one CETP fragment conjugate. Applicants respectfully traverse. Attention is drawn to the specification, pages 20 and 21. That section of the instant specification states:

> In another preferred embodiment, the immunizing DNA encodes a CETP immunogen that is comprised of an exogenous carrier to which *one or more*

immunogenic polypeptides having a length of about 10 to about 30 amino acid residues such as those of SEQ ID Nos: 2-7 or 50 having a sequence of rabbit CETP, the similar polypeptides of SEQ ID Nos: 8-13 or 29 having a sequence of human CETP or the similar polypeptides of SEQ ID Nos: 32-37 having a sequence of monkey CETP is covalently bonded. (emphasis added).

Therefore, it is respectfully submitted that the claims as amended find literal support in the specification, and it is respectfully requested that this rejection be removed.

2. Claims 3-11 and 15-27 were rejected under 35 U.S.C. § 112, first paragraph for containing new matter, in that the specification does not contemplate reducing HDL levels. This clerical error in the claims has been rewritten to require increasing HDL levels, and thus it is respectfully requested that this rejection, as to the claims as amended, be withdrawn.

Rejection Under 35 U.S.C. § 112, First Paragraph

Claims 1-11 and 15-31 stand rejected under 35 U.S.C. § 112, first paragraph, as lacking enablement. Specifically, the Examiner has contended that Table 1, at page 45 of the instant specification renders claims 1-11 and 15-31 inoperative.

35 U.S.C.§ 112, first paragraph states:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same, and shall set forth the best mode contemplated by the inventor of carrying out his invention.

In the instant application, claims 1-11 and 15-31 are directed to:

I. a method of raising antibodies to CETP (claims 1, 4, and 22);

II. an inoculum (claims 17-21and 28);

III. a recombinant DNA molecule (claims 29-31); and

IV. increasing the concentration of HDL in the blood of a mammal by:

"(a) immunizing said mammal with an inoculum containing a vehicle in which is dissolved or dispersed a CETP immunogen that is a fusion protein of (i) an exogenous antigenic carrier polypeptide..." and

"(c) repeating said immunizing step until the HDL cholesterol value in the blood of said mammal is increased to about 10 percent relative to the HDL cholesterol value prior to said first immunization step." (claims 3, 2, 5-11, 15-16, and 23-27)

A careful reading of the specification reveals that Example 2 (p. 43-46), and in particular Table 1, only represents antibodies and HDL values for the first-immune sera (*not* the boosted sera). Thus, Table 1 represents a comparison of pre-immune sera and first-immune sera. Table 1 illustrates that even after a single inoculation, a measurable increase occurs in HDL levels.

The procedure for Example 2 is specified on pages 43-44:

> "This study utilized 30 New Zealand white rabbits in three groups with 10 rabbits per group. Three immunogens were utilized in this study: (1) Recombinant human CETP, (2) the carboxy-terminal 26 amino acid residues of rabbit CETP (SEQ ID NO:50), and (3) a control immunogen whose amino acid residue sequence was unrelated to that of CETP.
>
> Pre-immune sera were collected before immunization with the respective immunogens. The purpose of this study was to illustrate that the above CETP immunogens would induce anti-CETP-specific (autogeneic anti-CETP) antibodies in rabbits, and that the autogeneic antibodies generated against CETP bind to (immunoreact with) the endogenous rabbit CETP, and thus lessen the transfer of cholesteryl esters from HDL particles and raise the level of HDL in the hosts.
>
> The above immunogens were emulsified in CFA. Each rabbit received 500 μg of one of the immunogens emulsified in CFA immunized by sub-cutaneous route. Seven weeks later *the first bleed post-immune sera were collected.*
>
> ***

> The results of this study on the elevation of HDL particle concentration in the blood (plasma) of the host mammals (mean ±.S.D.) are shown in Table 1, below, *for those first-immune sera.*" (emphasis added).

In contrast, Example 1 (p.40-42) describes immunizing rabbits with multiple inoculations of immunogen.

However, the claims at issue require "repeating said immunization step until the HDL cholesterol value in the blood of said mammal is increased by about 10 percent..." While Example 2 states that more immunizations were later performed, Table 1 does not represent those data. Therefore, the claims in question, 3, 2, 5-11, 15-16, and 23-27, are not merely enabled by Table 1 in isolation, but rather are enabled by *all* of the examples.

Furthermore, those claims that are unrelated to Table I (for raising HDL cholesterol), i.e. claims 1, 4, and 22 (a method of raising antibodies to CETP); claims 17-21 and 28 (a human inoculum); and ; claims 29-31 (a recombinant DNA molecule) are not properly subject to this rejection.

It is thus respectfully asserted that the rejection under 35 U.S.C. § 112, first paragraph is improper. The PTO cannot make this [lack of enablement] rejection unless it has reason to doubt the objective truth of the statements contained in the written description. See In re Brana, 51 F.3d 1560,1566, 34 USPQ2d 1436, 1441 (Fed. Cir. 1995) ("[T]he PTO has the initial burden of challenging a presumptively correct assertion of utility in the disclosure. Only after the PTO provides evidence showing that one of ordinary skill in the art would reasonably doubt the asserted utility does the burden shift to the applicant to provide rebuttal evidence sufficient to convince such a person of the invention's asserted utility."); see also In re Marzocchi, 439 F.2d 220, 223, 169 USPQ

367, 369 (CCPA 1971) ("[A] specification disclosure which contains a teaching of the manner and process of making and using the invention in terms which correspond in scope to those used in describing and defining the subject matter sought to be patented must be taken as in compliance with the enabling requirement of the first paragraph of § 112 unless there is reason to doubt the objective truth of the statements contained therein which must be relied on for enabling support."). The PTO may establish a reason to doubt an invention's asserted utility when the written description "suggest[s] an inherently unbelievable undertaking or involve[s] implausible scientific principles." Brana, 51 F.3d at 1566, 34 USPQ2d at 1441; see also In re Eltgroth, 419 F.2d 918, 164 USPQ 221 (CCPA 1970) (control of aging process).

In the instant application, there is ample enabling disclosure of the methods of claims 3, 2, 5-11, 15-16, and 23-27, including the procedure for Example 1 on pages 40-43.

Furthermore, the Examiner has not presented evidence to refute the enablement of repeatedly immunizing a mammal with an inoculum containing a vehicle in which is dissolved or dispersed a CETP immunogen until the HDL cholesterol value in the blood of said mammal is increased to about 10 percent relative to the HDL cholesterol value prior to a first immunization.

It is therefore respectfully requested that the rejection under 35 U.S.C. § 112, first paragraph be removed, and the case be passed to issue.

Rejection Under 35 U.S.C. § 112, First Paragraph

Claims 1-11 and 16-31 were rejected under 35 U.S.C. § 112, first paragraph as lacking enablement, in that the enumerated sequences are not commensurate with the scope of the claims. Applicants respectfully traverse this rejection.

The specification gives operative examples of sequences known to be both antigenic and antagonistic to CETP. In order to fall within the scope of claims 1-11 and 16-31, as amended, the CETP immunogen must both raise antibodies and increase HDL cholesterol. Because those skilled in the art would appreciate that certain CETP amino acid residue sequences raise antibodies and are antagonistic with respect to CETP biological activity, Applicants are entitled to the full scope of these claims.

Rejection Under 35 U.S.C. § 112, First Paragraph

Claims 1-11 and 15-28 were rejected as indefinite because claims 1 and 3 recite a recombinant DNA molecule which is dissolved or dispersed in a vehicle, but it was unclear how individual nucleotides could be dissolved or dispersed in a vehicle. The amendments to claims 1, 3, and 17 now all require containing a recombinant DNA (as opposed to "dissolved or dispersed"). It is believed that any indefiniteness found in the claims is therefore obviated by this amendment.

Rejection Under 35 U.S.C. § 102(b)

Claims 17 and 29 stand rejected under 35 U.S.C. § 102(b) as anticipated by Jeong, NW et al. 1994, IDS #A26 ("Jeong").

Claim 17 has been amended to include the limitation of a human inoculum, encoding a human CETP residue.

Jeong does not teach a human inoculum. Therefore, 35 U.S.C. § 102(b) is now inapplicable to claim 17 as amended, and it is respectfully requested that the rejection under 35 U.S.C. § 102(b) be withdrawn.

Claim 29 has been amended to include the limitation of a " CETP amino acid residue sequence of about 10 to 30 residues." Jeong does not teach a CETP amino acid residue sequence of about 10 to 30 residues. Therefore, 35 U.S.C. § 102(b) is now inapplicable to claim 29 as amended and it is respectfully requested that the rejection under 35 U.S.C. § 102(b) be withdrawn.

Rejection Under 35 U.S.C. § 103

Claims 18-21, 29 and 30 stand rejected as being unpatentable over Jeong NW et al. 1994, IDS #A26 in view of Bujard , et al., U.S. patent No. 5,650,298 ("Bujard").

Claims 18-21 depend from claim 17. Claim 17 has been amended to include the limitation of a human inoculum, encoding a human CETP residue.

In order to establish a *prima facie* case of obviousness, the Office must first show that the prior art relied upon, coupled with the knowledge generally available in the art at the time of the invention, contains some suggestion or incentive that would have motivated the skilled artisan to modify a reference or to combine references. See *In re Fine*, 5 U.S.P.Q.2d 1596, 1598 (Fed. Cir. 1988.

Next, the Office must show that the proposed modification of the prior art must have had a reasonable expectation of success, determined from the vantage point of the

skilled artisan at the time the invention was made. See *Amgen, Inc. v. Chugai Pharm. Co.,* 18 U.S.P.Q.2d 1016, 1023 (Fed. Cir. 1991).

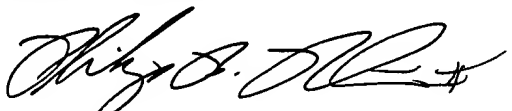
Finally, the prior art reference or combination of references must teach or suggest all the limitations of the claims. See *In re Wilson,* 165 U.S.P.Q.494, 496 (C.C.P.A. 1970).

Jeong does not teach a human inoculum, and Bujard does not suggest combining with or modifying Jeong in such a way as to make claims 18-21 obvious.

Claim 29 is independent, and claim 30 depends from claim 29. Claim 29 has been amended to include the limitation of a " CETP amino acid residue sequence of about 10 to 30 residues." Jeong does not teach a CETP amino acid residue sequence of about 10 to 30 residues, and Bujard does not suggest combining with or modifying Jeong in such a way as to make claims 29 and 30 obvious.

Neither Jeong alone nor in combination with Bujard teaches or suggests the inventions of amended claims 18-21, 29 and 30. It is respectfully requested that claims 18-21, 29 and 30 be passed to issue.

Respectfully submitted,



Philip B. Polster II, Reg. No. 43,864
Polster, Lieder, Woodruff & Lucchesi, L.C.
763 South New Ballas Road, Suite 230
St. Louis, Missouri 63141
(314) 872-8118